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PATENT EXAMINING OPERATION

Applicant(s): Glen H. ERIKSON et al.

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Group Art Unit: 1637

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Att. Docket No.: E1047/20044

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For: QUADRUPLEX DNA AND DUPLEX PROBE SYSTEMS

REQUEST FOR RECONSIDERATION AFTER ENTRY OF RCE

Box RCE
Commissioner for Patents
Washington, DC 20231

Sir:

In response to the Advisory Action dated December 2, 2002 and in further response to the Final Rejection dated May 30, 2002, favorable reconsideration is respectfully requested in view of the following remarks.

Claims 1-52 are pending, with claims 26-49 and 52 being withdrawn from consideration pursuant to a restriction requirement.

Claims 1-25 and 50-51 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing non-enabled subject matter. Claims 1-25 and 50-51 also stand rejected under 35 U.S.C. § 101, as allegedly lacking patentable utility. These rejections are respectfully traversed.

The December 2, 2002 Advisory Action at page 4 states:

Applicants' arguments and the declaration provided, did not substantially [overcome] the rejection under 35 U.S.C. 112 first paragraph, enablement. X-ray [crystallographic] or space filling model evidence supporting W-C base pairing involving more than two strands would [overcome] the rejection. The rejection

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under 35 U.S.C. 101 is based on the rejection under 35 U.S.C. 112 first paragraph, enablement. It will be maintained since Applicants did not overcome the rejection under 35 U.S.C. 112 first paragraph. [Emphasis added.]

Accordingly, the attached Information Disclosure Statement (IDS) cites the following references:

- (1) McGavin, "Models of Specifically Paired Like (Homologous) Nucleic Acid Structures," J. Mol. Biol. (1971) 55, 293-298 (hereinafter "McGavin 1");
- (2) McGavin, "Relationships and Transformations Between Some Nucleic Acid Models," J. Theor. Biol. (1980) 85, 665-672 (hereinafter "McGavin 2");
- (3) McGavin, "Four Strand Recombination Models," J. Theor. Biol. (1989) 136, 135-150 (hereinafter "McGavin 3");
- (4) McGavin, "Four-Strand Structure, Kinks and Cruciforms in DNA," J. Theor. Biol. (1989) 138, 117-128 (hereinafter "McGavin 4"); and
- (5) McGavin et al., "A Computer Graphics Study of Multistranded DNA Models," J. Mol Graphics. (1989) 7, 218-232 (hereinafter "McGavin 5").

which were published in scholarly journals, and show "space filling model evidence supporting W-C base pairing involving more than two strands."

The references track the development of theoretical multiplex nucleic acid models by Stewart McGavin of the University of Dundee (Scotland) over almost twenty years of research.

McGavin 1 discloses a theoretical model for quadruplex nucleic acid sequences based on the Watson-Crick base tetrads depicted on pages 293-95. McGavin 1 proposes models for the assembly of these previously postulated tetrads into nucleic acid sequences, wherein the tetrads are "stacked on top of each other." McGavin 1 at 293. According to McGavin 1 at the fifth full paragraph on page 296:

Preliminary work with models (Courtauld space filling) shows that there is no difficulty in building four-stranded structures in which two helices of the Watson-Crick-Wilkins type are related by a dyad axis parallel to the long molecular axis (Plate I).

Plate I of McGavin 1 is a photograph of the resulting "space filling model."

McGavin 2 further elaborates on the earlier publication, and at page 668 mentions the possibility of three-stranded structures based on the same kind of Watson-Crick "bonding system." Although McGavin 2 refers back to Plate I of McGavin 1 for a photograph of the four-strand model, Fig. 1 of McGavin 2 is a photograph of the "core structure" of the space-filling model.

McGavin 3 "develop[s] the idea that synapsis of DNA duplexes might take place by Watson-Crick base pairing between essentially intact duplex structures to form the same regular and compact

four strand structure already discussed" in McGavin 1 and 2. See the Abstract of McGavin 3. Figs. 1 and 2 of McGavin 3 contain additional depictions of four-stranded nucleic acids based on Watson-Crick base interaction.

McGavin 4 discloses computer graphic models of four-stranded nucleic acids based on Watson-Crick base interaction. In the Introduction, the models are specifically distinguished from the "homopolynucleotide" structures disclosed by, e.g., Sen et al., Nature, 334, 364-66 (1988), which Applicants have previously distinguished from their invention.

McGavin 5 contains more detailed computer graphic models of four-stranded nucleic acids based on Watson-Crick base interaction, including the "basic four-strand structure" first described in McGavin 1. Color Plate 2(a) shows the computer-generated model corresponding to the original space-filling model of McGavin 1. The computer modeling of McGavin 5 adds quantitative support to the earlier postulated space-filling models. For example, McGavin 5 reports at page 231:

The total energy of the four-strand model itself is slightly lower than twice that of either of its duplex components taken separately (that is, than two components of the Watson-Crick kind or two components of the "alternative" kind (2c)). The four-strand structure involves more interactions of the van der Waals kind, and also of the electrostatic kind, than the sum of two components of either kind taken separately.

Such quantitative calculations suggesting the thermodynamic favorability of four-stranded Watson-Crick complexes lend further

credence to the existence of such complexes and the invention claimed by Applicants.

In view of the fact that Applicants have complied with the Office's request for models supporting W-C base pairing involving more than two strands by providing several independently authored references from several different scholarly journals showing quadruplex and triplex models based on Watson-Crick base interaction, reconsideration and withdrawal of the pending rejections are respectfully requested.

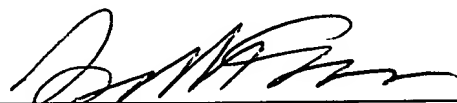
For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

If this response is not deemed to place the application in condition for allowance, Applicants respectfully request that the Examiner telephone the undersigned to schedule a personal interview at the United States Patent and Trademark Office before a further Office Action is issued.

Respectfully submitted,

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February 3, 2003

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